Supplementary Data

The modulated structure of a tricyclic natural product-like compound of empirical formula $C_{22}H_{20}O_3$

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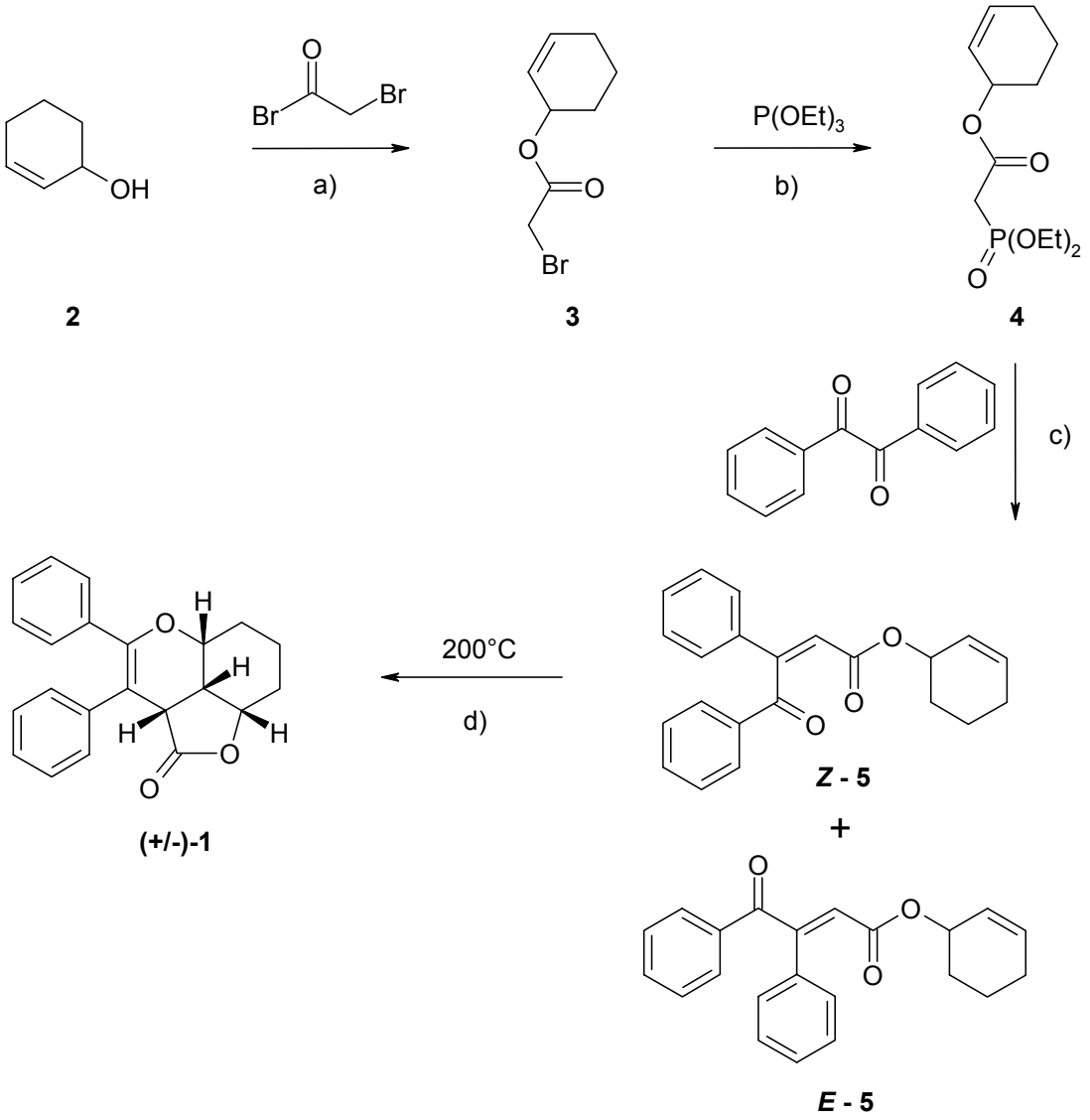

Scheme 1. Synthesis of 3,4-diphenyl-2a,5a,6,7,8,8a,8b-heptahydro-furo[4,3,2de]chromen-2-one (**1**); a) CH_2Cl_2, pyridine, 1h, 0°C → rt, 1h, 78%. b) THF, reflux, 19h, 83%. c) *n*-BuLi, hexamethyldisilazane (HMDS), THF, -70°C, 3h, 90%. d) Autoclave, toluene, 17 h, 41%.

Experimental Section

General. Chemicals, solvents, and reagents for reactions were from Acros, Aldrich, or Fluka, and were of the highest quality available. Solvents for extraction and chromatography were of technical grade and distilled prior to use. Thin layer chromatography (TLC): silica-gel 60 F_{254} glass plates (Merck); visualisation by UV and/or by dipping into a solution of vanillin (8.6 g) and conc. H_2SO_4 (2.5 ml) in EtOH (200 ml) followed by heating. Flash column chromatography (CC): Silica 60 A C.C 40-63 µm (SDS, France) at low pressure. Melting points were determined in open capillaries using a *Büchi Melting Point B-545* apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR: Bruker AVANCE 300, δ values in ppm (solvent signals as internal standards), *J* [Hz]; ^{31}P-NMR: Bruker AVANCE 300, δ values in ppm (85% H_3PO_4 as external standard).

Infrared spectra were recorded on an *OMNILAB Jasco FT/IR-460 Plus* spectrophotometer with a *Specac MK II Golden Gate™ Single Reflection ATR System*. EI-MS: Micromass Autospec Q (*Waters / Micromass*), Ionization mode: electron impact, Ionization energy: 70 eV, Sample inlet: solids probe, Acceleration voltage: 8 kV, Mass resolving power: >1000 (10% valley), Calibration: External calibration using perfluorokerosene (PFK). Autoclave: A high pressure reactor made of high-alloy, SS 316 TI stainless steel with PTFE lining by *Berghof* was used. Type: HR-100; 150 ml, 100 bar, 250°C. The autoclave is equipped with a rupture disc to reliably limit maximum pressure, clamping ring for tool-free opening and closing, thermometer, pressure gauge and sample extraction device.

Bromoacetic acid cyclohex-2-enyl ester (3). A solution of bromoacetyl bromide (0.44 ml, 5.1 mmol) in CH_2Cl_2 (1 ml) was added dropwise to a stirred solution of racemic 2-cyclohexen-1-ol (**2**, 0.50 ml, 5.1 mmol) and pyridine (0.45 ml, 5.6 mmol) in CH_2Cl_2 (5 ml) at 0°C under a nitrogen atmosphere. Directly after the addition of bromoacetyl bromide the colour changed to white later yellow and formation of a solid was visible. The obtained suspension was allowed to warm to room temperature during one hour. The mixture was poured onto saturated aqueous ammonium chloride and extracted three times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and concentrated. The liquid product was separated from a small amount of brown residue by removal with a pipette. The obtained bromoacetic acid cyclohex-2-enyl ester (**3**, 0.865 g, 78%) was used without further purification. TLC (EtOAc/hexane, 1:8): R_f 0.68. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 6.00 (m, 1H), 5.71 (m, 1H), 5.30 (m, 1H), 3.82 (s, 2H), 2.16-1.57 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 167.0 (s), 133.8 (d), 124.8 (d), 70.3 (d), 28.1 (t), 26.5 (t), 24.9 (t), 18.7 (t). EI-MS *m/z* (%): 220 ($[C_8H_{11}O_2{}^{81}Br]^+$, weak), 218 ($[C_8H_{11}O_2{}^{79}Br]^+$, weak), 139 (84), 98 (83), 97 (89), 81 (94), 80 (90), 79 (100), 70 (84), 41 (97), 39 (83). IR (cm^{-1}): 1726, 1273.

(Diethoxy-phosphoryl)-acetic acid cyclohex-2-enyl ester (4). Triethyl phosphite (0.48 ml, 2.8 mmol) was added to a solution of bromoacetic acid cyclohex-2-enyl ester (**3**, 0.40 g, 1.83 mmol) in dry THF (3.5 ml) under a nitrogen atmosphere. The light brown solution was stirred and refluxed for 19 h. Then THF and triethyl phosphite were removed in vacuo. (Diethoxy-phosphoryl)-acetic acid cyclohex-2-enyl ester (**4**, 0.417 g, 83%) was isolated and used without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 5.93 (m, 1H), 5.68 (m, 1H), 5.27 (m, 1H), 4.14 (m, 4H), 2.93 (d, 2H, $^2J_{HP}$=21.5 Hz), 2.12-1.52 (m, 6H), 1.31 (t, 6H, *J*=7.1 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 165.6 [s (d, 1C, $^2J_{CP}$=6.2 Hz)], 133.2 (d), 125.2 (d), 69.4 (d), 62.7 [t (d, 2C, $^2J_{CP}$=6.2 Hz)], 34.7 [t (d, 1C, $^1J_{CP}$=133.6 Hz)], 28.2 (t), 24.9 (t), 18.8 (t), 16.4 [q (d, 2C, $^3J_{CP}$=6.2 Hz)]. ^{31}P-NMR (121 MHz, $CDCl_3$): δ 20.0 (s, 1P). EI-MS *m/z* (%): 276 ($[C_{12}H_{21}PO_5]^+$, 7), 197 (58), 179 (68), 169 (58), 152 (82), 151 (75), 125 (71), 123 (86), 81 (61), 79 (100). IR (cm^{-1}): 1726, 1259, 1047, 1018, 962, 912.

(*E*/*Z*)-4-Oxo-3,4-diphenyl-but-2-enoic acid cyclohex-2-enyl ester (5). HMDS (0.18 ml, 0.87 mmol) was added slowly to a stirred solution of *n*-butyllithium (0.5 ml, 0.80 mmol, 1.6 M solution in hexane) in dry THF (2.5 ml) at 0°C under a nitrogen atmosphere. After half an hour, (diethoxy-phosphoryl)-acetic acid cyclohex-2-enyl ester (**4**, 0.200 g, 0.72 mmol) dissolved in dry THF (1 ml) was added to the solution. Then the solution was cooled down to -70°C and benzil (0.167 g, 0.80 mmol) dissolved in dry THF (1 ml) was added slowly. For the final half hour the cooling bath was removed. After 3 hours, the solution was poured onto saturated aqueous ammonium chloride and extracted three times with

EtOAc. The combined organic phases were dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (EtOAc/hexane, 1:10) and (*E*/*Z*)-4-oxo-3,4-diphenyl-but-2-enoic acid cyclohex-2-enyl ester (**5**, 0.180 g, 90%) was isolated as a yellow oily liquid. The ratio of the *E*- and *Z*-isomer was 35:65 (as determined by NMR). TLC (EtOAc/Hexane, 1:10): R_f 0.36 (both *E*- and *Z*-isomer). ^{1}H-NMR (300 MHz, $CDCl_3$, mixture of isomers): δ 7.98-7.90 (m, 4H), 7.60-7.32 (m, 16H), 6.52 (s, 1H, *E*), 6.28 (s, 1H, *Z*), 5.94-5.83 (m, 2H), 5.66-5.52 (m, 2H), 5.25-5.18 (m, 2H), 2.03-1.43 (m, 12H). EI-MS *m/z* (%): 332 ($[C_{22}H_{20}O_3]^+$,19), 105 (99), 77 (100), 51 (96).

3,4-Diphenyl-2a,5a,6,7,8,8a,8b-heptahydro-furo[4,3,2-de]chromen-2-one (1). The reaction was carried out in an autoclave. (*E*/*Z*)-4-Oxo-3,4-diphenyl-but-2-enoic acid cyclohex-2-enyl ester (**5**, 171 mg, 0.51 mmol) was dissolved in dry toluene (17 ml) and placed in a Teflon® reaction chamber inside a sealed steel autoclave. The autoclave was heated in an oil bath and kept at an inside temperature of 184-187°C for 17 h. The solvent was removed in vacuo and the product was purified by column chromatography (EtOAc/hexane, 1:4). 3,4-Diphenyl-2a,5a,6,7,8,8a,8b-heptahydro-furo[4,3,2-de]chromen-2-one (**1**, 69 mg, 41%) was isolated as a white solid. For X-ray analysis the compound was recrystallised from EtOH. Besides the product, unreacted *E*-4-oxo-3,4-diphenyl-but-2-enoic acid cyclohex-2-enyl ester (***E*-5**, 67 mg, 39%) was also isolated. TLC (EtOAc/Hexane, 1:4): R_f 0.24. ^{1}H-NMR (300 MHz, DMSO): δ 7.27-7.16 (m, 10H), 4.75 (m, 1H), 3.98 (d, 1H, *J*=9.0 Hz), 3.90 (m, 1H), 3.11 (m, 1H), 2.27-2.12 (m, 2H), 1.77-1.45 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 178.2 (s), 156.2 (s), 139.6 (s), 134.4 (s), 129.2 (d), 129.1 (d), 128.7 (d), 128.5 (d), 128.0 (d), 126.8 (d), 116.9 (s), 76.2 (d), 74.9 (d), 47.1 (d), 44.1 (d), 28.8 (t), 27.4 (t), 13.2 (t). EI-MS *m/z* (%): 332 ($[C_{22}H_{20}O_3]^+$, 74), 105 (100), 77 (66). IR (cm^{-1}): 1755, 1168, 1055, 980, 743, 693, 667; mp (EtOH): 185°C.